Pulmonary Mechanics during General Anesthesia:

V. Status Asthmaticus

Martin I. Gold, M.D., and Martin Helrich, M.D.

Six patients in status asthmaticus were given halothane anesthesia. Two patients breathed spontaneously and four received mechanical ventilation during the two to three hours of anesthesia. All patients improved subjectively following this procedure, and this improvement continued. Measurements of pulmonary mechanics and blood gases did not reflect improvement either during or immediately after treatment. However, blood gas and resistance values during IPPB moved clearly towards normal values. Cardiac arrhythmias and bronchospasm occurred after tracheal intubation in more than half of the patients. The temporal relationship to tracheal intubation is particularly significant. General anesthesia must be considered radical therapy, potentially dangerous and not justified by favorable changes in pulmonary compliance, resistance or blood gas values.

GENERAL ANESTHESIA has been used to treat status asthmaticus,[1-5] but it is potentially dangerous.[6] Upper airway obstruction, especially during induction, may complicate the existing extreme respiratory difficulty. Hypotension or cardiac arrhythmias associated with depression of various organ systems may ensue. There are few reports concerning the use of halothane in the treatment of status asthmaticus.[7, 8] However, it has been used successfully to manage the asthmatic patient during elective surgery.[9, 10] Evidence suggests that it relaxes smooth muscle,[11] causes minimal secretions,[12] and is associated with increases in bronchial caliber and pulmonary compliance.[13] Diethyl ether, traditionally used in the treatment of status asthmaticus, has been criticized for producing copious tracheobronchial secretions.[9, 10] Consequently, halothane has sometimes been chosen as the general anesthetic. This agent has beta-adrenergic stimulating activity,[14] and in dogs given histamine or vagal stimulation, has proved to be a significantly more potent bronchodilator than cyclopropane.[15]

The present investigation was designed to evaluate the effects of halothane and tracheal intubation on pulmonary mechanics and blood gases in six patients in status asthmaticus. All were women, some had been in attacks for as long as three weeks, and each had been treated for at least 72 hours. Multiple courses of epinephrine, aminophylline, steroids, antibiotics and inhaled isoproterenol during both spontaneous and intermittent positive-pressure breathing had been tried.

The hazards of anesthesia and the fact that this was an investigation were explained thoroughly to each patient and her family and informed consent was obtained.

Methods

All patients were considered similar with respect to disease, prior treatment, method of investigation and immediate postanesthetic care. One difference was that patients A, B and C were studied on consecutive postanesthetic days and returned to a Clinical Study Center, facilitating measurement of pulmonary mechanics on post-treatment days. Patients D, E and F were returned to their medical beds and discharged within 24 hours. The original protocol was to determine the effects of halothane anesthesia, administered to spontaneously-breathing patients in a stepwise manner in concentrations from 0.5 through 2.0 per cent. Because of the circulatory and respiratory complications of patients A and B, the protocol was changed, and patients C, D, E and F received IPPB during anesthesia (concentration of inhaled halothane averaged between 0.5 and 1.5 per cent).

Without premedication, an esophageal balloon was passed into the middle third of the esophagus with topical anesthesia. Pulmonary compliance (C_L, l/cm H_2O), resistance (R_L,

Received from the Department of Anesthesiology, University of Maryland Hospital and School of Medicine, Baltimore, Maryland. Accepted for publication January 26, 1970. Supported in part by USPHS Grants HE-06429 and RR 33.

TABLE 1. Pulmonary Mechanics and Blood Gases before, during and after "Treatment" in Supine Asthmatic Patients

Stage of Experiment	Patient	R_L (cm H_2O/l/sec)	C_L (l/cm H_2O)	V_T (ml)	f (/min)	$P_{A_{O_2}}$ (mm Hg) Air	$P_{A_{O_2}}$ (mm Hg) 50 % O_2	$P_{a_{O_2}}$ (mm Hg)	Arterial Halothane (mg)/100 ml
1. Control. Patients conscious, mouthpiece in place, spontaneous respiration	A	33.9	0.037	495	13	69	218	35	
	B	46.3	0.038	445	18	60	221	45	
	C	43.0	0.055	466	16	64	207	40	
	D	16.1	0.028	340	34	52	191	41	
	E	12.2	0.085	484	18	62	128	36	
	F	16.7	0.044	372	24	50	178	35	
	MEAN	28.0	0.048	434	20	60	190	39	
	SEM	6.1	0.008	26	3	3	14	2	
2. From tracheal intubation to "treatment." Patients anesthetized, endotracheal tube in place, spontaneous respiration	A	28.0	0.034	296	32		164	54	2.8
	B	56.2	0.019	128	37		89	130	
	C	20.4	0.059	204	34		134	58	
	D	33.6	0.016	127	48		84	78	11.6
	E	12.2	0.100	355	26		168	42	6.3
	F	9.2	0.100	166	40		207	44	9.7
	MEAN	26.6	0.055	213	36		141	68	7.6
	SEM	7.0	0.016	38	3		20	14	1.9
3. During "treatment." Patients anesthetized, endotracheal tube in place, spontaneous respiration	A	30.6	0.034	196	36		168	44	6.6
	B	43.7	0.040	177	33		136	115	
	MEAN	37.2	0.037	186	34		152	80	
	SEM	6.6	0.003	10	2		16	36	
Patients anesthetized, endotracheal tube in place, IPPB	C	24.7	0.028	444	25		136	43	
	D	14.5	0.038	574	22		246	33	19.2
	E	12.3	0.073	648	17		113	32	8.3
	F	16.7	0.047	470	23		229	38	12.7
	MEAN	17.0	0.046	534	22		181	36	13.4
	SEM	2.7	0.010	47	2		33	3	3.2
4. After "treatment." Patients anesthetized, endotracheal tube in place, spontaneous respiration	A	21.1	0.029	208	31		134	42	7.1
	B	54.4	0.035	206	29		166	99	
	C	53.7	0.031	231	33		64	102	
	D	15.7	0.020	126	57		80	71	7.0
	E	12.0	0.081	391	23		162	40	2.7
	F	21.2	0.031	210	29		77	41	4.4
	MEAN	29.7	0.038	229	34		114	66	5.3
	SEM	7.8	0.009	36	5		19	12	1.1
5. Patients emerging from anesthesia. Conscious, mouthpiece in place, spontaneous respiration	A	19.4	0.084	636	12				
	B	46.8	0.020	222	33	47		91	
	C	34.2	0.020	567	16	73		50	
	D	27.9	0.030	212	30				
	E	11.2	0.102	540	18	80		40	1.6
	F	12.5	0.067	419	34	43		41	3.3
	MEAN	25.3	0.054	433	24	61		56	2.4
	SEM	5.6	0.014	74	4	9		12	0.8

	Patient	1st Day R_L	1st Day C_L	2nd Day R_L	2nd Day C_L	3rd Day R_L	3rd Day C_L
6. Post-anesthesia. Patients conscious, mouthpiece in place, spontaneous respiration	A	28.1	0.038	24.5	0.046	16.1	0.048
	B	14.9	0.082	7.2	0.132		
	C	10.6	0.085	10.8	0.078		
	MEAN	17.9	0.068	14.2	0.085		
	SEM	5.3	0.015	5.3	0.025		

TABLE 2. Chronology in Minutes

Patient	Stage of Experiment							
	Control 1	Induction to Tracheal Intubation	2	"Treatment" 3	4	Halothane Off to Tracheal Extubation	5	Induction to End of Study
A	17	12	28	95	45	17	6	203
B	17	8	45	91	29	8	12	193
C	20	10	60	60	25	5	9	169
D	12	12	17	39	17	43	6	134
E	13	9	17	78	7	11	4	126
F	13	8	7	172	8	29	5	229
MEAN	15	10	29	89	22	19	7	164

cm H_2O/l/sec), Pa_{O_2}, Pa_{CO_2} and arterial halothane values were obtained simultaneously and analyzed by methods previously described.[16-19] An Analytic Systems ultraviolet halothane analyzer calibrated with an F and M flame ionization chromatograph[19] was used to monitor inhalation and exhalation concentrations, while oxygen was monitored with a Beckman D-2 analyzer.

After control measurements (mouthpiece, noseclip) induction of anesthesia began (100 mg thiopental intravenously in patient E and halothane, 50 per cent nitrous oxide–oxygen in a semiclosed circle system in the other five). Anesthesia was maintained with halothane in nitrous oxide–oxygen, and in each patient the trachea was intubated within 12 minutes of induction. After tracheal intubation, measurements were made as follows: during spontaneous respiration after a relative steady state existed with respect to auscultatory blood pressure, pulse, respiratory rate (f), tidal volume

TABLE 3. Complications and Blood Gases Relative to Tracheal Intubation

Patient	Minutes after Induction	Comment	Cardiac Arrythmia	Bronchospasm	Pa_{O_2} (mm Hg)	Pa_{CO_2} (mm Hg)
A	12	Tracheal intubation,	—	Yes	—	—
	15	coughing at various times	Yes 10 min		119	61
	25	—	No	48 min		
	35	—	—		208	47
	60	—	—	No	167	48
B	8	Tracheal intubation,	—	Yes	—	—
	12	coughing throughout entire	Yes 33 min	approx. 160 min	54	105
		period of intubation	No			
	45	—	—		89	150
	181	Extubation	—	No	—	—
D	12	Tracheal intubation	—	—	—	—
	16	—	—	Yes 35 min	79	77
	32	Succinylcholine, IPPB	—		—	—
	51	—	—	No	241	31
F	8	Tracheal intubation	—	—	—	—
	11	—	—	Yes	207	44
	14	Succinycholine, IPPB	—		—	—
	28	—	Yes 12 min	55 min	228	66
	40	—	No		—	—
	66	—	Yes 19 min	No	240	38
	85	—	No	—	—	—

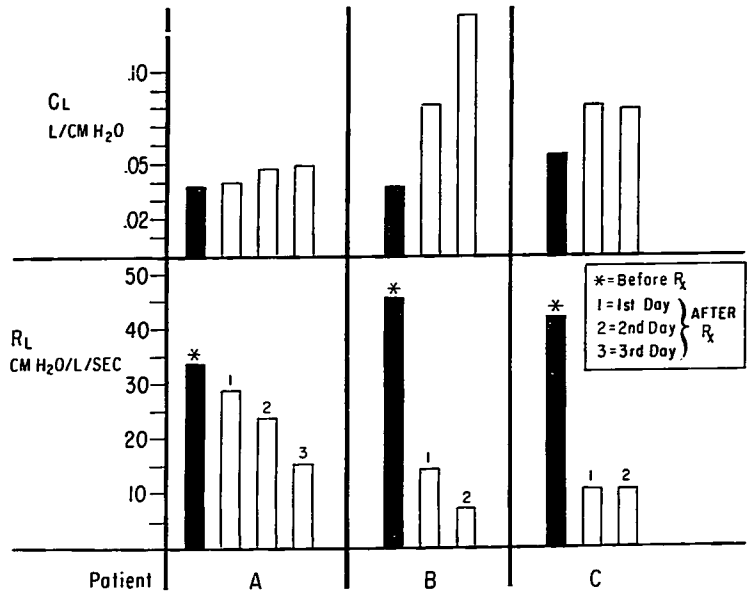

FIG. 1. Pre- and post-treatment pulmonary mechanics.

(V_T), and inhaled and exhaled concentrations of halothane; during "treatment," consisting of spontaneous breathing in patients A and B and IPPB in patients C, D, E and F; during spontaneous respiration with halothane, nitrous oxide–oxygen; during spontaneous respiration after halothane and nitrous oxide had been stopped, when the patients were awake enough to use the mouthpiece and noseclip as they had before anesthesia. Secretions were aspirated from the tracheobronchial tree by way of the endotracheal tube during anesthesia at necessary, and occasionally frequent, intervals.

All patients were taken to the recovery room and each had IPPB with aerosolized isoproterenol (0.25 per cent) administered by mask for five minutes during each hour. Warm, humidified air was inhaled during spontaneous breathing. Postural drainage and chest physiotherapeutic techniques were provided during the remainder of the hospitalization. Postanesthetic medical management included only those modalities used prior to anesthesia.

Results

Mean R_L, C_L, V_T, f, Pa_{O_2} (inhaling air and 50 per cent O_2), Pa_{CO_2}, and arterial halothane levels are shown in table 1. Duration in minutes of each stage of the experiment is shown in table 2.

All patients had elevated R_L and decreased C_L with relatively normal V_T and Pa_{CO_2}, whereas only patient D had an elevated f value, prior to therapy. During "treatment" (table 1) patients A and B, compared with patients C, D, E and F, had higher R_L, lower V_T, more rapid f, lower Pa_{O_2} and higher Pa_{CO_2} (paired variate t test, $P > 0.05$). Comparison of values immediately before and after treat-

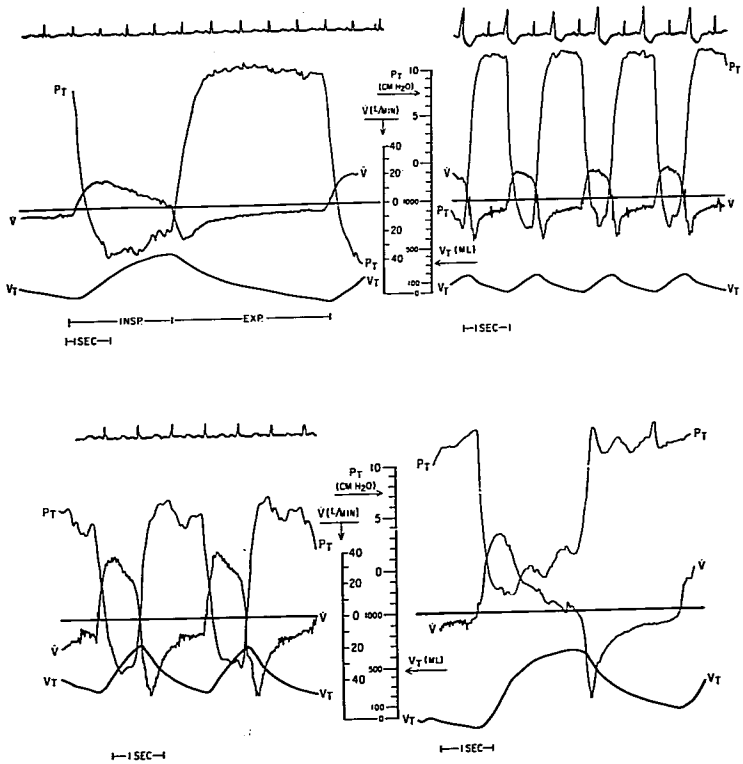

FIG. 2. Above, left. Awake control, breathing spontaneous through mouthpiece in status asthmaticus, RL 34, prolonged expiration. Above, right. Anesthetized, breathing spontaneous immediately after tracheal intubation. Note tachypnea and ventricular premature systoles with bigeminy. Below, left. Anesthetized, after 2¾ hours of halothane anesthesia Below, right. Awake 15 minutes, breathing spontaneous through mouthpiece after extubation, RL (19), patient "feels fine."

ment (table 1, stages 2 and 4) showed little change.

Table 1, stage 6 shows the pulmonary mechanics data for patients A, B and C on post-treatment days. Table 3 shows the sequences of the two serious complications, bronchospasm and cardiac arrhythmia. Bronchospasm, which occurred in four patients, is defined as a period of difficult inflation, wheezing during inspiration with prolonged expiration, with or without coughing, bucking and straining in the nonapneic state. Patients A, B and F developed cardiac arrhythmias, primarily premature ventricular contractions, lasting ten to 30 minutes. The arrhythmias occurred three or four minutes after intubation in patients A and B and 20 minutes after intubation in patient F.

Figure 1 depicts the pulmonary mechanics values of patients A, B and C on consecutive

post-"treatment" days. Figure 2 shows individual scalar traces of transpulmonary pressure (P_T), flow rate (V), and V_T in patient A before, during and after anesthesia.

Discussion

The six asthmatic patients were in severe status asthmaticus, and ineffectual medical management led to the administration of general anesthesia as a therapeutic measure. No patient was retaining carbon dioxide; the ability of an asthmatic patient to increase alveolar ventilation during an attack has been reported.[20] On the other hand, the mean control Pa_{O_2} of 60 mm Hg during the inhalation of air is low in the presence of normal alveolar ventilation (mean Pa_{CO_2} 39 mm Hg) but may be explained as a consequence of ventilation–perfusion ratio abnormalities.[20-22] No significant change ($P > 0.05$) in any parameter was demonstrated when awake control values were compared with the postanesthetic values (table 1, stages 1 and 5). It is possible that the total cross-sectional area of the tracheobronchial tree was reduced in the control state because of smooth-muscle spasm, and after anesthesia because of a flood of secretions. Either condition creates elevated resistance.

Patients A and B, who breathed spontaneously throughout anesthesia, hypoventilated, but both improved subjectively postanesthetically, as did patients C, D, E and F. However, the cardiac arrhythmias and bronchospasm coinciding with the hypoventilation in both patients were sufficient cause for altering therapy. IPPB as a part of the treatment of status asthmaticus has been reported.[7, 8, 23] The V_T and f used during IPPB were similar to those values during the awake control state, and similar Pa_{CO_2} values reflect the similarity in alveolar ventilation. The Pa_{CO_2} values during IPPB were more physiologic than those during spontaneous breathing; the two highest recorded Pa_{O_2} values also occurred during IPPB. In an animal study, decreasing R_L coincided with increasing halothane levels,[14] a phenomenon not noted in patients A and B. The mobilization and removal of secretions by aspiration following tracheal intubation and subsequent to extubation cannot be discounted as a factor in their improvement.

The use of tracheal intubation as a routine procedure during general anesthesia for asthmatic patients has been criticized.[9] The physiology related to foreign bodies in the tracheobronchial tree, stimulation of the cough reflex, and the complex autonomic nervous system pathways involved[24, 25] lend support to this admonition. In this investigation intubation was not attempted until sufficient depth of anesthesia had been attained. The diagnosis of bronchospasm and its relationship to tracheal intubation were based on judgment and objective measurements. However, there was no consistent correlation between the difficult inflation following tracheal intubation and the values for pulmonary mechanics or blood gases. Bronchospasm was related temporally to the act of tracheal intubation, occurring either at that time or within four minutes.

Cardiac arrhythmias, primarily premature ventricular contractions, were self-limited, lasting ten to 33 minutes. It is possible that the release of catecholamines during relatively light anesthesia was related to the development of these arrhythmias. However, in no instance did the blood pressure increase in an alarming fashion, nor was there the expected relief of bronchospasm from a theoretically-high blood level of "endogenous catecholamines." In two of the three instances, arrhythmias bore no relationship to abnormal blood gases, but patient B developed an alarmingly high Pa_{CO_2}.

References

1. Thompson, H. T., Pryor, W. J., and Hill, J.: Bronchial lavage in the treatment of obstructive lung disease, Thorax 21: 557, 1966.
2. Williams, N. E., and Crooke, J. W.: The practical management of severe status asthmaticus, Lancet 1: 1081, 1968.
3. Sweatman, C. A.: Treatment of bronchial asthma and hay fever with cyclopropane, J. S. Carolina Med. Ass. 37: 291, 1941.
4. Schotz, S., and Meyer, N. E.: Relief of severe intractable bronchial asthma with cyclopropane, J. Allerg. 10: 239, 1938–39.
5. Fuchs, A. M.: The interruption of the asthmatic crisis by tribromethanol (Avertin), J. Allerg. 8: 340, 1937.
6. Bendixen, H. H., Egbert, L. D., Hedley-Whyte, J., Laver, M. B., and Pontoppidan, H.: Respiratory Care. St. Louis, C. V. Mosby, 1965, pp. 218.

7. Broom, B.: Intermittent positive-pressure respiration and therapeutic bronchial lavage in intractable status asthmaticus, Lancet 1: 899, 1960.
8. Ambiavagar, M., and Jones, E. S.: Resuscitation of the moribund asthmatic, Anaesthesia 22: 375, 1967.
9. Shnider, S. M., and Papper, E. M.: Anesthesia for the asthmatic patient, ANESTHESIOLOGY 22: 886, 1961.
10. Gold, M. I., and Helrich, M.: A study of the complications related to anesthesia in asthmatic patients, Anesth. Analg. 42: 283, 1963.
11. Brown, D.: Halothane–oxygen anaesthesia for bronchoscopy, Anaesthesia 14: 135, 1959.
12. Morrow, R. C., Reed, E. M., and Abajian, J.: Application of fluothane anesthesia to otolaryngological surgery, Laryngoscope 71: 545, 1961.
13. Colgan, F. J.: Performance of lungs and bronchi during inhalation anesthesia, ANESTHESIOLOGY 26: 778, 1965.
14. Klide, A. M., and Aviado, D. M.: Mechanism for the reduction in pulmonary resistance induced by halothane, J. Pharmacol. Exp. Ther. 158: 28, 1967.
15. Hickey, R. F., Graf, P. D., Nadel, J. A., and Larson, C. P., Jr.: The effects of halothane and cyclopropane on total pulmonary resistance in the dog, ANESTHESIOLOGY 31: 334, 1969.
16. Wells, R. E., Jr.: Mechanics of respiration in bronchial asthma, Amer. J. Med. 26: 384, 1959.
17. Gold, M. I., and Helrich, M.: Pulmonary compliance during anesthesia, ANESTHESIOLOGY 26: 281, 1965.
18. Gold, M. I., and Helrich, M.: Mechanics of breathing during anesthesia: 2. The influence of airway adequacy, ANESTHESIOLOGY 26: 751, 1965.
19. Gold, M. I., Han, Y. H., and Helrich, M.: Pulmonary mechanics during anesthesia: III. Influence of intermittent positive pressure and relation to blood gases, Anesth. Analg. 45: 631, 1966.
20. McFadden, E. R., Jr., and Lyons, H. A.: Arterial-blood gas tension in asthma, New Eng. J. Med. 278: 1027, 1968.
21. Rees, H. A., Millar, J. S., and Donald, K. W.: Adrenaline in bronchial asthma, Lancet 2: 1164, 1967.
22. Rees, H. A., Borthwick, R. C., Millar, J. S., and Donald, K. W.: Aminophylline in bronchial asthma, Lancet 2: 1167, 1967.
23. Misuraca, L.: Mechanical ventilation in status asthmaticus, New Eng. J. Med. 275: 318, 1966.
24. Tomari, Z., and Widdicombe, J. G.: Muscular bronchomotor and cardiovascular reflexes elicited by mechanical stimulation of the respiratory tract, J. Physiol. 200: 25, 1969.
25. Simonsson, B. G., Jacobs, F. M., and Nadel, J. A.: Role of autonomic nervous system and the cough reflex in the increased responsiveness of airways in patients with obstructive airway disease, J. Clin. Invest. 46: 1812, 1967.

Drugs

ASPIRIN AND BLEEDING TIME The technique for a standardized, reproducible Ivy bleeding time is described and used to compare the effects of aspirin and those of a placebo on the bleeding times of 60 normal male subjects. Following 1 g of aspirin orally, the mean bleeding time was 9 min, 30 sec, compared with 5 min, 30 sec after placebo and 5 min in the control state. The difference between the mean bleeding times after placebo and after aspirin was highly significant statistically. The data support the conclusion that small amounts of aspirin may exert significant effects upon hemostasis in normal individuals. (*Mielke, C. H., and others: The Standardized Normal Ivy Bleeding Time and Its Prolongation by Aspirin, Blood 34: 204 (Aug.) 1969.*)

ANTIVENIN FOR PANCREATITIS Acute hemorrhagic pancreatitis was established in dogs by injection of bile under pressure. This is thought to allow pancreatic enzymes to penetrate the interstitium and initiate the pancreatitis. Pancreatic enzymes are closely related chemically and immunologically to those in snake venom. The control animals had 100 per cent mortality in 17 hours. Animals treated with a polyvalent antivenin survived an average of 27 hours, and a quarter of the group survived several days. The mechanism of the protective effect of antivenin has not been established. (*Rittenbury, M., and Hanback, L.: Snake Antivenin, Arch. Surg. 99: 179 (Aug.) 1969.*)